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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/035,637	11/07/2001	Yashwant M. Deo	MXI-166CP	4452

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EXAMINER	
EWOLDT, GERALD R	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/035,637	DEO ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *27-35,38,39,42-46 and 49-51* is/are pending in the application.

4a) Of the above claim(s) *42-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *27-35,38,39 and 49-51* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 42-46 stand withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to non-elected inventions.

Claims 27-35, 38, 39, and newly added Claims 49-51, read on the elected invention and are being acted upon.

2. Applicant's amendment and remarks filed 05/10/05 are acknowledged. In view of the amendment, the previous rejections under 35 U.S.C. 102(b) and 103(a) have been withdrawn.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 31, 34, 38, and 39 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

As set forth previously, There is insufficient written description to show that Applicant was in possession of the "conservative sequence modifications" of the molecular conjugates of Claims 31 and 34.

The specification neither defines the term nor discloses any of the modified conjugates of the claims. Given the essentially unlimited number of compositions encompassed by the claims, one of skill in the art would conclude that the specification fails to disclose a representative number of species to describe the claimed genus. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

Applicant has not addressed this rejection.

5. Claims 31, 34, 38, and 39 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

As set forth previously, Given the established unpredictability of the art, the instant specification would require a significant teaching to be enabled. In particular, it is unlikely that the generic modified conjugates encompassed by the claims could function for their intended use. Note that the modified conjugates of the claims would encompass conjugates modified in the CDR binding regions of the antibody portions of the conjugates. It is well-established that even single substitutions in the CDR regions of an antibody can have a dramatic, and unpredictable, effect on antibody binding (and thus, function). See, for example, Kobayashi et al. (1999) wherein it is taught that even single conserved substitutions can have a large effect on antibody binding (see Figure 4; note the log scale). Note the breadth of the claims; the conjugates of the claims are not limited in the number of modifications/substitutions allowed. Thus, even antibodies in which *all* of the amino acids are changed would be encompassed by the claims.

The instant specification provides no examples of the modified conjugates of the instant claims. Accordingly, one of ordinary skill in the art must conclude that the specification fails to adequately disclose how to make and use the claimed invention. Accordingly, the invention is considered to be highly unpredictable and requiring of undue experimentation to practice as claimed.

Applicant's arguments filed 5/10/05 have been fully considered but they are not persuasive. Applicant argues, "This phrase [conservative substitutions] would be readily understood by a skilled practitioner as referring to modifications that do not substantially affect or alter the binding characteristics of the antibody containing the claimed amino acid sequence. Conservative substitutions are well known in the art and are understood to include amino acids in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Such families of amino acid residues having similar side chains are well known in the art." Applicant argues that substituted antibodies can be tested employing routine assays.

It is noted that Applicant has not addressed the meat of the rejection. The Examiner has *shown* that even single conserved substitutions can effect binding. Applicant merely argues that substitutions (random, multiple, all residues?) can be made and the resulting antibodies can be tested for activity. It appears that the Declarant is arguing that the skilled artisan might simply employ a method of trial-and-error to establish which substituted antibodies might be functional. It is the Examiner's position that more is required, e.g., some guidance as to which residues might be expected to accept substitutions and which might not. As methods of trial-and-error employing randomly substituted antibodies would provide no particular expectation of success with any particular antibody, the use of such methods are considered to comprise undue experimentation.

6. The following are new grounds for rejection necessitated by Applicant's amendment.

7. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 27-30, 32, 33, 35, 38, 39, 50, and 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,922,845 (IDS) in view of Tuting et al. (1998, of record) and Sallusto et al. (1995).

The '845 patent teaches a molecular conjugate comprising an antibody that binds to dendritic cells (DCs) (FcαR) and an antigen, wherein said antigen comprises a component of a pathogen or a tumor (cancer) antigen (see column 3, lines 49-59). The reference further teaches the conjugate comprising a single chain antibody (see column 3, line 63), a pharmaceutically acceptable carrier (see column 4, line 32), and an adjuvant (see column 21, line 54. The reference further teaches that the molecular conjugates of the reference can be used to "harness the capabilities of white blood cells", e.g., phagocytosis, for "enhancing the attack of these cells against cancer cells, cells of infectious microorganisms, and cells infected with pathogens".

The reference teaching differs from the claimed invention only in that it does not teach a molecular conjugate comprising an antibody that binds to a human macrophage mannose receptor and the Pmel-17 tumor antigen.

Tuting et al. teaches that Pmel-17 is one of several well known melanoma antigen (see particularly page 1140, column 1).

Sallusto et al. teaches that the human mannose macrophage receptor (which would be encoded by SEQ ID NO:7) can be employed for the uptake of antigen by DCs for presentation of said

antigen to T cells (see particularly Abstract; page 392, column 1; and Figure 4).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention to produce a molecular conjugate comprising an antibody that binds to white blood cells (which would include DCs) and tumor antigen, as taught by the '845 patent, employing an antibody that binds the human macrophage mannose receptor and Pmel-17 as the antigen. One of ordinary skill in the art at the time the invention was made would have been motivated to employ an antibody that binds the human macrophage mannose receptor because it is more APC-specific than is the FcαR of the '845 patent, thus allowing for more efficient antigen uptake by APCs and more efficient antigen presentation to T cells. One of ordinary skill in the art at the time the invention was made would have been motivated to employ any of the well known tumor antigens in an anti-cancer therapeutic agent, such as Pmel-17 as taught by Tuting et al., because of their availability and previous characterization.

9. Claims 27-30, 32, 33, 35, 38, 39, 50, and 51 are rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically:

A molecular conjugate comprising a human monoclonal antibody that binds to the human macrophage mannose receptor linked to an antigen (Claims 27 and 33).

Applicant indicates that support for the new limitation can be found at page 2 of the specification.

Page 2 of the specification discloses only the B11 antibody encoded by SEQ ID NOS: 2 and 4 and not the generic antibody of the claims.

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

12. Applicant's amendment or action necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Please Note: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

7/25/05

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600